

Endourology: A Basic Science and Clinical Update

*Highlights from the 22nd World Congress on Endourology and Shockwave Lithotripsy/
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The basic research symposium at the 2004 World Congress of Endourology meeting included sessions on tissue sealants and hemostasis, ureteral obstruction, shock wave lithotripsy (SWL) and metabolic evaluation, and urologic training in endourology and laparoscopy. The highlights of these sessions will be profiled below.

Tissue Sealants and Hemostasis

A number of adjuncts for partial nephrectomy and percutaneous ablation of renal tumors were presented at the tissue sealants and hemostasis session. Sur and associates¹ (Duke University, Durham, NC) assessed the efficacy of Bioglue® (CryoLife,

Kennesaw, GA), a bovine serum albumin and glutaraldehyde-based glue, and Crosseal™ (OMRIX Biopharmaceuticals, Brussels, Belgium), a fibrin glue, for hemostasis and primary closure of the collecting system in a porcine open surgical partial nephrectomy model. Bioglue was found to be effective for both, whereas Crosseal was not.

FloSeal™ (Baxter International, Deerfield, IL), a gelatin matrix hemostatic sealant, and Tisseel® (Baxter International), a fibrin glue, have been used for hemostasis and collecting system closure during partial nephrectomy and to prevent hemorrhage with tubeless percutaneous nephrolithotomy. Kim and colleagues² (University of California, Irvine, Irvine, CA) assessed the effects of injecting 2 mL of either one of these agents into the collecting system at the time of withdrawal of an acute

percutaneous nephrostomy tube in swine. The injection of either substance resulted in significant obstruction 5 days after injection. One should consider the implications of these results when considering the use of these agents in this setting or during partial nephrectomy.

Renal hypothermia can limit ischemic injury during partial nephrectomy when renal arterial circulation is interrupted. This might be difficult to achieve during laparoscopic partial nephrectomy. Ames and associates³ (Washington University School of Medicine, Saint Louis, MO) described a method of applying fine ice slush to the kidney with a novel deployment system. They were able to attain satisfactory renal cooling in swine with this approach. Laven and colleagues⁴ (University of Chicago Hospitals, Chicago, IL) reported on the use of a micro-particulate ice slurry for renal

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cooling in a porcine model. This preparation, which can be easily injected through ports with suction/irrigation probes, also resulted in satisfactory renal cooling.

Percutaneous or laparoscopic directed radiofrequency ablation (RFA) is currently used to treat selected patients with renal tumors. The renal collecting system can be injured when centrally located tumors are treated with RFA. Margulis and associates⁵ (The University of Texas South-

western Medical Center, Dallas, TX) assessed the ability of retrograde renal cooling delivered through a ureteral access sheath to limit collecting system injury during RFA of centrally located renal tissue in a porcine model. This significantly limited injury to the collecting system without compromising parenchymal destruction. Studies with longer follow-up periods are needed to better define the benefits of this adjunct because this was only an acute study.

Renal hypothermia can limit ischemic injury during partial nephrectomy when renal arterial circulation is interrupted, but this might be difficult to achieve during laparoscopic partial nephrectomy.

Real-time monitoring of renal lesions generated with RFA has not been described. Ogan and colleagues⁶ (Emory University, Atlanta, GA) described using contrast-enhanced ultrasonography during RFA in a porcine model and reported that the lesion depicted with this form of imaging correlated with that found on histologic analysis.

Ureteral Obstruction

The ureteral obstruction session provided insights into the effects and treatment of ureteral obstruction. Nakada and associates⁷ (University of Wisconsin-Madison, Madison, WI) reported that renal cyclooxygenase-2

expression is induced with acute ureteral obstruction and that this might be a stretch-induced phenomenon. This report was based on experiments in which acute ureteral obstruction was created in swine, and cultured human urothelial cells were subjected to cyclic stretching. This same group found that activation of the prostaglandin EP3 receptor plays a role in prostaglandin E2-mediated ureteral hypercontractility occurring during acute ureteral obstruction.⁸

Renal tubular and interstitial fibrosis develops after ureteral obstruction. Semerdzhiev and colleagues⁹ (Long Island Jewish Medical Center, New Hyde Park, NY) reported that this is linked to macrophage infiltration and that morphine attenuated this response in a murine model.

A number of pharmacologic agents have been reported to facilitate ureteral stone passage. Ames and associates¹⁰ (Washington University School of Medicine, Saint Louis, MO) reported that the intraureteral instilla-

tion of aminophylline inhibited ureteral peristalsis and that verapamil stimulated ureteral dilation in a porcine model. They propose that such pharmacologic manipulations might have a clinical role in future.

SWL and Metabolic Evaluation

submucosal graft or this preparation seeded with autologous bladder cells as a ureteral substitute in swine, as well as autologous bladder cells seeded on porcine acellular matrix in dogs, for this purpose. Unfortunately, all grafts were noted to be obstructed. Further such work in this important field is necessary because effective ureteral substitutes are needed.

An interesting array of papers was presented at the session concerning SWL and metabolic evaluation. Several addressed the pathophysiology of stone formation. Seo and colleagues¹² (Wonkwang University School of Medicine, Iksan Chonbuk, South Korea) reported that a vitamin D receptor polymorphism, BsmI, is more prevalent in subjects forming calcium-containing stones. The phenotypic influence of this polymorphism will need to be characterized.

Chuang and associates¹³ (University of Chicago Hospitals, Chicago, IL) described a rat model of enteric hyperoxaluria and stone formation. They found that calcium oxalate, apatite, and calcium carbonate crystals filled the collecting ducts, causing tubular obstruction and interstitial inflammation. This leads to papillary interstitial

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crystal deposition and papillary erosion, similar to histologic changes identified in humans with enteric hyperoxaluria and nephrolithiasis.

Low dietary calcium intake has been identified as a risk factor for stone formation in large epidemiologic studies. Matsumoto and colleagues¹⁴ (University of Texas Southwestern Medical Center, Dallas, TX) performed a controlled metabolic study in which normal subjects were administered a low

Efforts have been made in the past to use bioengineered tissue as a ureteral substitute. Marcovich and colleagues¹¹ (University of Texas HSC, San Antonio, TX) described using either a multilayer small intestinal

calcium (400 mg/day) and normal calcium diet (1000 mg/day) in random sequence. Oxalate and other dietary nutrients were similar in both phases. Whereas oxalate excretion was less with the 1000-mg calcium diet, calcium excretion and the relative supersaturation of calcium oxalate were greater. Further such studies need to be undertaken in a stone-forming population.

Investigators have shown that exposing cultured renal cells to supra-physiologic concentrations of oxalate and inducing extreme levels of hyperoxaluria in rats promote oxidative stress. It has been hypothesized that this might play a role in idiopathic calcium oxalate nephrolithiasis. Assimos and Holmes¹⁵ (Wake Forest University School of Medicine, Winston-Salem, NC) performed a study in which normal, non-stone-forming adults were administered 720 mg of sodium oxalate load-adjusted to 70 kg of body weight. Although oxalate excretion reached levels similar to those in patients with primary hyperoxaluria, there was no acute evidence of oxidative stress. This group is now performing similar studies in stone-forming patients.

Almost 90% of the Indian patients with staghorn stones had calcium oxalate calculi, which is distinctly different from the situation in North America.

Urinary studies are used to identify metabolic abnormalities in stone-forming patients. This information can be used to prescribe dietary modifications and pharmacotherapy in an effort to eradicate or attenuate stone activity. Accurate normal values of urinary analyte excretion are used to define "abnormal" results. Reddy and colleagues¹⁶ (Cincinnati Children's Hospital, Cincinnati, OH) assessed this in 51 non-stone-forming, normal children (mean age 8.8 years) and

found that urinary calcium, oxalate, and citrate excretion indexed to urinary creatinine were greater in children than in normal adults. This study demonstrates that adult values should not be used to determine normal values for children.

Stone disease is usually influenced by both dietary and environmental factors. These influences might vary across the world and cause diversity in stone composition and metabolic abnormalities among populations.

A progressive increase in lithotripter voltage produces better stone comminution and reduces renal injury.

Ansari and associates¹⁷ (All India Institute of Medical Science, New Delhi, India) reported that almost 90% of their patients with staghorn stones had calcium oxalate calculi, which is distinctly different from the situation in North America, where struvite, carbonate, and apatite are the common constituents. Shrivastav and colleagues¹⁸ (Muljibhai Patel Urological Hospital, Nadiad, India) performed a retrospective study of the metabolic abnormalities in 1050 patients with

vivo models (porcine) that a progressive increase in lithotripter voltage produces better stone comminution and reduces renal injury. This needs to be confirmed in humans. Li and colleagues²⁰ (Kaohsiung Medical University, Taiwan) demonstrated in an in vitro model that radiographic contrast and lower urinary specific gravity might attenuate shock wave stone comminution. Computed tomographic (CT) attenuation coefficients of stones are somewhat predictive of SWL stone

fragility. Refinements in this technology have permitted identification of internal stone structure. Kim and associates²¹ (Methodist/Clarian Hospital and Indiana University, Indianapolis, IN) used standard and micro-CT, a novel technology, to characterize the internal and topographic structure of cystine stones and found that stones that had an irregular surface with areas of low attenuation fragmented better with SWL in an in vitro setting than those that were homogenous and had a higher mean attenuation coefficient. This elegant work also awaits clinical verification.

Urologic Training in Endourology and Laparoscopy

A number of models have been developed to facilitate the learning of endourologic and laparoscopic surgery. Some were profiled in the surgical learning session. Margulis and associates²² (The University of Texas Southwestern Medical Center, Dallas, TX) validated the effectiveness of a virtual reality percutaneous renal access simulator (PERC Mentor™; Simbionix, Cleveland, OH). Residents and medical students were randomized to receive or not undergo initial training on this

stones and found that the prevalence of hyperoxaluria and hypocitraturia was significantly greater than in North American stone-forming populations.

Shock wave lithotripsy remains an effective and commonly used treatment for patients harboring renal or ureteral stones. We are continuing to learn how to better improve SWL results. Springhart and associates¹⁹ (Duke University, Durham, NC) demonstrated in both in vitro and in

apparatus before attempts at percutaneous access in swine. The trained cohort took less time, used less fluoroscopy, needed fewer puncture attempts, and perforated the collecting system less frequently than those without simulator training. Although such technology is costly, innovative and inexpensive models were also introduced during this session. Schwartz and Hammond²³ (Southern Illinois University, Springfield, IL) described the insertion of a porcine kidney into a chicken carcass and the use of this corpus to practice percutaneous renal access. Laguna and colleagues²⁴ (AMC University Hospital, The Netherlands) also described a "fowl" model for acquisition of skills for laparoscopic vesicourethral anastomosis. They have sutured chicken esophagus to stomach as a surrogate for this anastomosis.

The aforementioned studies are reflective of the many novel and innovative advances that are occurring in both the basic science and the clinical domains of endourology

and urologic laparoscopy. This work will undoubtedly improve our understanding of the disease processes of our patients and improve their care. ■

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Main Points

- The injection of 2 mL of either FloSeal or Tisseel into the collecting system at the time of withdrawal of an acute percutaneous nephrostomy tube in swine resulted in significant obstruction 5 days after injection.
- Retrograde renal cooling delivered through a ureteral access sheath to limit collecting system injury during radio-frequency ablation in a porcine model significantly limited injury to the collecting system without compromising parenchymal destruction.
- Renal tubular and interstitial fibrosis after ureteral obstruction has been linked to macrophage infiltration; morphine attenuated this response in a murine model.
- Investigators reported that intraureteral instillation of aminophylline inhibited ureteral peristalsis and that verapamil stimulated ureteral dilation in a porcine model.
- A study of 51 healthy children demonstrated that adult values of urinary analyte excretion should not be used to determine normal values for children; similarly, dietary and environmental factors might vary across the world and cause diversity in stone composition and metabolic abnormalities among populations.
- Standard and micro-computed tomography were used to characterize the internal and topographic structure of cystine stones; stones that had an irregular surface with areas of low attenuation fragmented better with shock wave lithotripsy than those that were homogenous and had a higher mean attenuation coefficient.
- Residents trained with a virtual reality percutaneous renal access simulator took less time, used less fluoroscopy, needed fewer puncture attempts, and perforated the collecting system less frequently than those without simulator training.

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